

Remarks

Claims 1-37 are pending. Claims 1, 5, 6, 10, 12, 14, 15, 18, 21, 23, 24, 27, 28, 29, 32 and 37 have been amended. The amendments to claims 1, 10 and 24 (step d) are supported by disclosure at page 4, paragraph 3 through page 5, paragraph 2 of the specification. The amendments to claims 23 and 24 (step e) are supported by disclosure at page 10, paragraph 2 of the specification. The amendments to claims 5, 6, 14, 15, 18, 21, 27, 28, 29, 32 and 37 are supported by the claims as originally filed. The amendment to claim 12 merely corrects a typographical error. No new matter has been added.

Rejections under 35 USC § 112

Claims 1-9, 14-15 and 21-37 are rejected under 35 USC § 112, second paragraph as being indefinite for various reasons. Applicants traverse.

1. Claims 1-9 are indefinite for reciting the limitation "a tissue/cell lysate" in claim 1. The Examiner indicates that it is unclear whether the "/" symbol means "and" or "or." Claim 1 has been amended to recite "a tissue or cell lysate."

2. Claims 5 and 6 are indefinite for reciting the limitation "animal and plant tissues and/or cells" in claim 5. According to the Examiner it is unclear whether "cells" includes those of animal and plant origin or if "cells" is an alternative to animal and plant tissues. Claim 5 has been amended to recite that the biological sample is selected from the group consisting of "animal tissues, plant tissues, animal cells, plant cells, and combinations thereof." Claim 6 has been amended to recite "animal tissues or cells."

3. Claims 14 and 15 are indefinite for reciting the limitation "said chaotropic agent." According to the Examiner, there is insufficient antecedent basis for this limitation. As suggested by the Examiner, claims 14 and 15 have been amended to recite "said one or more chaotropic agents."

4. Claims 21 and 22 are indefinite for reciting the limitation "said elution" in claim 21. According to the Examiner, there is insufficient antecedent basis for this limitation. As suggested by the Examiner, claim 21 has been amended to recite "eluting."

5. Claim 23 is indefinite for reciting the limitation "said eluting step." According to the Examiner, there is insufficient antecedent basis for this limitation. As suggested by the Examiner, claim 23 has been amended to remove the word "step."

6. Claims 24-37 are indefinite for reciting the limitation "a tissue/cell lysate" in claim 24. The Examiner indicates that it is unclear whether the "/" symbol means "and" or "or." Claim 24 has been amended to recite "a tissue or cell lysate."

7. Claims 27-29 are indefinite for reciting the limitation "said lysis buffer" in claim 27. According to the Examiner, there is insufficient antecedent basis for this limitation. As suggested by the Examiner, claim 27 has been amended to recite "a lysis buffer."

8. Claims 28 and 29 are indefinite for reciting the limitation "said chaotropic agent." According to the Examiner, there is insufficient antecedent basis for this limitation. As suggested by the Examiner, claims 28 and 29 have been amended to recite "said one or more chaotropic agents."

Applicants believe that the amendments to the claims render the claims clear and definite. Therefore, Applicants request reconsideration and withdrawal of the rejections under 35 USC § 112, second paragraph.

Rejections under 35 USC § 102

1. Claims 1-8 are rejected under 35 USC § 102(b) as being anticipated by Colpan *et al.* (U.S. Pat. No. 6,383,393). According to the Examiner, Colpan *et al.* teach a method of preparing a sample substantially free of genomic DNA by forming a tissue/cell lysate from a biological sample; contacting a pre-filtration column with said lysate, wherein said pre-filtration column comprises a filter material, wherein said filter material has at least one layer

of glass; and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA. Applicants traverse.

Claim 1 has been amended to include filtering the collected effluent from the pre-filtration column through a silicon carbide whisker column. Colpan *et al.* do not disclose a method of preparing a sample essentially free of genomic DNA by utilizing a silicon carbide whisker column. Therefore, Colpan *et al.* do not teach each and every element of claim 1 as currently pending. Claims 2-8 depend from claim 1, either directly or indirectly, and therefore necessarily include all of the elements of claim 1. Thus, claims 1-8, as currently pending, are novel over Colpan *et al.*, and this rejection should be withdrawn.

2. Claim 9 is rejected under 35 USC § 102(b) as being anticipated by Colpan *et al.* (U.S. Pat. No. 6,383,393) as defined by the Aldrich Catalog (at page T289 (1998/1999)). According to the Examiner, Colpan *et al.* teach the method of claim 1 and the use of glass fibers. Aldrich teaches glass fibers in 2 in. diameter bundles that are 22 feet long, weighing 454 g. Applicants traverse.

As discussed above, claim 1 has been amended to include filtering the collected effluent from the pre-filtration column through a silicon carbide whisker column. Colpan *et al.* do not disclose a method of preparing a sample essentially free of genomic DNA by utilizing a silicon carbide whisker column. Therefore, Colpan *et al.* do not teach each and every element of claim 1 as currently pending. Claim 9 depends from claim 1, and therefore necessarily includes all of the elements of claim 1. Thus, claim 9, as currently pending, is novel over Colpan *et al.*, and this rejection should be withdrawn.

Rejections under 35 USC § 103

1. Claims 10-17 and 19-22 are rejected under 35 USC § 103(a) as being unpatentable over Haj-Ahmad (U.S. Pat. No. 6,177,278) in view of Colpan *et al.* According to the Examiner, Haj-Ahmad teaches a method of isolating a nucleic acid from a sample matrix by forming a sample preparation by disrupting cells contained in said sample matrix using a lysis buffer; contacting a silicon carbide column with said sample preparation; and eluting said nucleic acid from said silicon carbide column. Haj-Ahmad teaches lysing of cells, but is silent with respect to tissues. However, Colpan *et al.* teach a method for isolating nucleic acid from a sample matrix by using a column to purify the nucleic acid after forming a lysate

from a biological sample including all tissues with the added benefit of allowing the study of tumors. The Examiner reasons that it would have been obvious to a person of ordinary skill in the art to modify the method of Haj-Ahmad to include the lysing of tissues as taught by Colpan *et al.* with a reasonable expectation of success, and that the ordinary artisan would have been motivated to do so because the modification would have resulted in allowing the study of tumors. Applicants traverse.

Claim 10 has been amended to incorporate the limitation from originally filed claim 18, which clarifies that the silicon carbide column is a silicon carbide whisker column. Neither Colpan *et al.* or Haj-Ahmad teach or suggest using silicon carbide whiskers. Moreover, the silicon carbide whiskers perform significantly different than the silicon carbide grit or powder used by Haj-Ahmad. Therefore, it is not obvious to substitute whiskers for the grit or powder material. Claims 11-17 and 19-22 depend from claim 10, either directly or indirectly, and thus necessarily include all of the elements of claim 10. Therefore, claims 10-17 and 19-22, as currently pending, are non-obvious over Haj-Ahmad in view of Colpan *et al.*, and Applicants request reconsideration and withdrawal of this rejection.

2. Claims 10 and 18 are rejected under 35 USC § 103(a) as being unpatentable over Colpan *et al.* and Haj-Ahmad in view of Kimura *et al.* (U.S. Pat. No. 3,933,984). According to the Examiner, claim 10 is obvious in view of Colpan *et al.* and Haj-Ahmad as previously discussed. In addition, the Examiner notes that Colpan *et al.* also teach fritted columns with layers adjacent to frits. The Examiner concedes that neither Haj-Ahmad nor Colpan *et al.* teach silicon carbide whiskers. However, the Examiner cites that Kimura *et al.* teach that the term "whisker," as applied to metal carbides, refers to needle-like single crystals having a diameter of a few microns and a length of several millimeters, thereby establishing the term "whisker" as a mere descriptor of the dimensions of the silicon carbide particles. Thus, the Examiner quotes that courts have held that "where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device." (Citation omitted). Applicants respectfully disagree.

Claim 10 has been amended to clarify that the silicon carbide column is a silicon carbide whisker column. The nucleic acid isolation described by Haj-Ahmad involves the use of silicon carbide grit, non-porous, irregularly shaped particles of a relatively low specific

surface area. In contrast, silicon carbide whisker has a comparatively high specific surface area for nucleic acid isolation. The silicon carbide whisker material used by the Applicants is 3.9 m²/g while the silicon carbide grit used by Haj-Ahmad is 0.4 m²/g as measured by surface Nitrogen absorption. The larger surface area of the silicon carbide whiskers is particularly effective for isolation of RNA from complex samples. It provides for at least double the yield of isolated nucleic acids compared to that of silicon carbide powder. Additionally, the larger surface area provides for isolating intact, *i.e.* less fragmented, RNA than the method described by Haj-Ahmad. Therefore, the whisker column performs significantly different than the particle column used by Haj-Ahmad, and thus is patentably distinct. Claim 18 depends from claim 10, and therefore necessarily includes all of the elements of claim 10. Applicants assert that claims 10 and 18 are non-obvious over Colpan *et al.* and Haj-Ahmad in view of Kimura *et al.*, and request reconsideration and withdrawal of this rejection.

3. Claims 24-31 and 33-36 are rejected under 35 USC 103(a) as being unpatentable over Colpan *et al.* in view of Haj-Ahmad. In brief, the Examiner states that it would have been obvious to a person of ordinary skill to have modified the method of isolation as taught by Colpan *et al.* by using a silicon carbide column as taught by Haj-Ahmad with a reasonable expectation of success. The Examiner reasons that the ordinary artisan would have been motivated to make the modification because it would have resulted in a column composed of an affordable and readily available substance in a variety of grades, each grade having a different capacity for binding nucleic acids. Applicants traverse.

Claim 24 has been amended to incorporate the limitation from originally filed claim 32, which clarifies that the silicon carbide column is a silicon carbide whisker column. Haj-Ahmad does not teach or suggest using silicon carbide whiskers. As discussed previously, the whisker material provides for significant improvements in the quantity and quality of isolated nucleic acids over the material used by Haj-Ahmad. The disclosure of Colpan *et al.* does not cure this deficiency. Claims 25-31 and 33-36 depend from claim 24, either directly or indirectly, and thus necessarily contain all of the limitations of claim 24. Therefore, claims 24-31 and 33-36, as currently pending, are non-obvious over Colpan *et al.* in view of Haj-Ahmad, and Applicants request reconsideration and withdrawal of this rejection.

4. Claims 24 and 32 are rejected under 35 USC 103(a) as being unpatentable over Colpan *et al.* in view of Haj-Ahmad in view of Kimura *et al.* for reasons identical to those

outlined for a similar rejection of claims 10 and 18 discussed previously. Applicants respectfully disagree.

As in claim 10, claim 24 has been amended to clarify that the silicon carbide column is a silicon carbide whisker column. The nucleic acid isolation described by Haj-Ahmad involves the use of silicon carbide grit, non-porous, irregularly shaped particles of a relatively low specific surface area. In contrast, silicon carbide whisker has a comparatively high specific surface area for nucleic acid isolation. The silicon carbide whisker material used by the Applicants is 3.9 m²/g while the silicon carbide grit used by Haj-Ahmad is 0.4 m²/g as measured by surface Nitrogen absorption. The larger surface area of the silicon carbide whiskers is particularly effective for isolation of RNA from complex samples. It provides for at least double the yield of isolated nucleic acids compared to that of silicon carbide powder. Additionally, the larger surface area provides for isolating intact, *i.e.* less fragmented, RNA than the method described by Haj-Ahmad. Therefore, the whisker column performs significantly different than the particle column used by Haj-Ahmad, and thus is patentably distinct. Claim 32 depends from claim 24, and therefore necessarily includes all of the elements of claim 24. Applicants assert that claims 24 and 32 are non-obvious over Colpan *et al.* and Haj-Ahmad in view of Kimura *et al.*, and request reconsideration and withdrawal of this rejection.

5. Claims 10, 23, 24 and 37 are rejected under 35 USC 103(a) as being unpatentable over Colpan *et al.* and Haj-Ahmad in view of Crossway *et al.* (U.S. Pat. No. 4,996,144). Neither Colpan *et al.* nor Haj-Ahmad teaches digestion with DNase. According to the Examiner, Crossway *et al.* teach a method of purification of nucleic acids using digestion with DNase with the added benefit of allowing differential detection of RNA only. Applicants traverse.

As discussed previously, claims 10 and 24 have been amended to clarify that the silicon carbide column is a silicon carbide whisker column. Neither Colpan *et al.* or Haj-Ahmad teach or suggest using silicon carbide whiskers. Moreover, the silicon carbide whiskers perform significantly different than the silicon carbide grit or powder used by Haj-Ahmad. Therefore, it is not obvious to substitute whiskers for the grit or powder material. The disclosure of Crossway *et al.* does not cure this deficiency. Claim 23 depends from claim 10 and claim 37 depends from claim 24. Therefore, claims 10, 23, 24 and 37 as

currently pending, are non-obvious over Colpan *et al.* and Haj-Ahmad in view of Crossway *et al.*, and Applicants request reconsideration and withdrawal of this rejection.

Statutory Double Patenting

Claim 25 is provisionally rejected under 35 USC § 101 as claiming the same invention as that of claim 13 of copending Application No. 10/914,920. Applicants respectfully disagree.

Claim 25 is directed to a method of isolating nucleic acids comprising forming a tissue or cell lysate from a sample matrix, contacting a pre-filtration column with the lysate, collecting effluent from the pre-filtration column, contacting a silicon carbide whisker column with the effluent, and eluting nucleic acid from the silicon carbide whisker column, wherein the nucleic acid is RNA. In contrast, claim 13 of the '920 application is directed to a method of preparing an RNA sample from a tissue comprising homogenizing a tissue sample, contacting a prefiltration column with the homogenate to obtain an RNA containing solution, contacting an RNA isolation column with the solution of RNA, and eluting the RNA from the RNA isolation column. Applicants contend that the RNA isolation column of claim 13 of the '920 application is not necessarily identical to the silicon carbide whisker column of claim 25 herein. Therefore, the claims do not encompass the same invention. Applicants request reconsideration and withdrawal of the rejection.

Nonstatutory Double Patenting

1. Claims 24, 30 and 32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 7-12 of copending Application No. 10/914,920 in view of Haj-Ahmad. According to the Examiner, both sets of claims are drawn to methods of purification of RNA using pre-filtration columns having a glass or borosilicate layer and contacting the effluent with a second column that allows separation of RNA. Claims 1 and 7-12 of the '920 application are silent with respect to silicon carbide, however Haj-Ahmad teaches purification of RNA using silicon carbide particles. The Examiner concludes that it would have been obvious to modify the claims of the '920 application with the silicon carbide particles as taught by Haj-Ahmad with a reasonable expectation of success, and the ordinary artisan would have been so motivated

because the modification would have resulted in use of an economically efficient medium for use in purification of nucleic acids. Applicants traverse.

Claim 24 has been amended to clarify that the silicon carbide column is a silicon carbide whisker column. Haj-Ahmad does not teach or suggest using silicon carbide whiskers. As discussed previously, the whisker material provides for significant improvements in the quantity and quality of isolated nucleic acids over the material used by Haj-Ahmad. Therefore, modifying the claims of the '920 application with the silicon carbide particles as taught by Haj-Ahmad does not result in the methods of pending claims 24, 30 and 32 herein. Thus, claims 24, 30 and 32 are non-obvious over the '920 application in view of Haj-Ahmad. Applicants request reconsideration and withdrawal of this rejection.

2. Claims 24 and 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 19 of copending Application No. 10/693,428 in view of Haj-Ahmad. According to the Examiner, both sets of claims are drawn to forming a tissue/cell lysate, contacting a prefiltration column with said lysate, wherein said prefiltration column comprises a filter material with at least one layer of glass or borosilicate fiber, collecting an effluent from said column, contacting the effluent with a second column, and collecting the nucleic acid from said second column. Claim 19 of the '428 application is silent with respect to silicon carbide, however Haj-Ahmad teaches purification of RNA using silicon carbide particles. Applicants traverse.

Claim 24 has been amended to clarify that the silicon carbide column is a silicon carbide whisker column. Haj-Ahmad does not teach or suggest using silicon carbide whiskers. As discussed previously, the whisker material provides for significant improvements in the quantity and quality of isolated nucleic acids over the material used by Haj-Ahmad. Therefore, modifying the claim 19 of the '428 application with the silicon carbide particles as taught by Haj-Ahmad does not result in the methods of pending claims 24 and 25 herein. Thus, claims 24 and 25 are non-obvious over the '428 application in view of Haj-Ahmad. Applicants request reconsideration and withdrawal of this rejection.

No fees are believed to be due with the filing of this amendment. However, if any fees are deemed to be necessary, the Commissioner is hereby authorized to charge any deficiencies to or credit any overpayment to Deposit Account No. 03-2410, Order No. 29830-102.

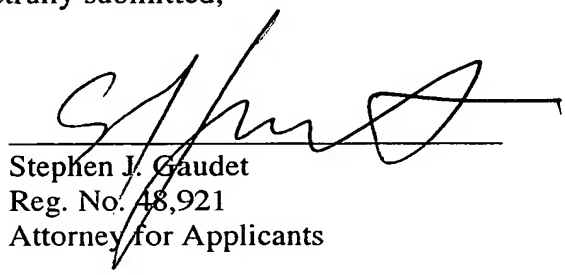
In accordance with Section 714.01 of the M.P.E.P., the following information is presented in the event that a call may be deemed desirable by the Examiner:

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